

## **Division of Adult Translational Research and Treatment Development (DATR)**

The Division of Adult Translational Research and Treatment Development (DATR) plans, supports, and administers programs of research, research training, and resource development aimed at understanding the pathophysiology of mental illness and hastening the translation of behavioral science and neuroscience advances into innovations in clinical care. The Division supports a broad research portfolio, which includes studies of the phenotypic characterization and risk factors for major psychiatric disorders; clinical neuroscience to elucidate etiology and pathophysiology of these disorders; and psychosocial, psychopharmacologic, and somatic treatment development. In addition, the Division supports an integrated program to clarify the psychopathology and underlying pathophysiology of psychiatric disorders of late life and to develop new treatments for these disorders. The focus of DATR is to support research on the etiology and pathophysiology of mental illness in order to:

- Define predictors and understand the mechanism of treatment response.
- Create and refine biomarkers, behavioral assessments, and phenotypic characterizations of disease.
- Evaluate existing therapeutics for new indications, and, in collaboration with academic, industry, and regulatory agencies, hasten the development of more effective new treatments for mental illness.

### **Division Offices and Branches**

Small Business Innovation Research (SBIR) Program and the Small Business Technology Transfer (STTR) Program (AT-BI)

Research Training and Career Development Program (AK-TN)

Traumatic Stress Disorders Research Program (AD-TS)

Adult Psychopathology and Psychosocial Intervention Research Branch (A2-AI)

Clinical Neuroscience Research Branch (A3-NS)

Geriatrics Research Branch (A4-GP)

Experimental Therapeutics Branch (A5-ET)

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## **Small Business Innovation Research (SBIR) Program and the Small Business Technology Transfer (STTR) Program (AT-BI)**

The Small Business Innovation Research (SBIR) Program supports research and development by small businesses of innovative technologies that have the potential to succeed commercially or to provide significant societal benefits. The Small Business Technology Transfer (STTR) Program has the same objectives but requires academic research involvement. In this Division, the SBIR and STTR Programs support research aimed at facilitating the validation and commercialization of new methods of assessing psychopathology, measuring treatment response to therapeutic agents or approaches, and the clinical development of novel psychopharmacological or psychosocial approaches to the treatment of mental illness.

### **Areas of Emphasis**

- Targeted projects to advance development of novel therapeutics.
- Development of novel methods to enhance efficiency of early phase clinical trials.
- Development of novel assessments of psychopathology suitable for use in clinical research.
- Development of biomarkers and/or predictors of treatment response or side effects of therapeutics to promote individualized treatment.

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## **Research Training and Career Development Program (AK-TN)**

The Research Training and Career Development Program supports research training at the pre-doctoral, post-doctoral, and early investigator levels of career development in areas relevant to the focus of the Division. These include adult psychopathology and psychosocial interventions, clinical neuroscience, geriatrics, translational research focusing on adults, and experimental therapeutics and treatment mechanisms related to mental illness. The primary goal of this office is to ensure that sufficient numbers of highly trained, independent investigators will be available to address the complexities of adult psychopathology and translational research.

### **Programs**

Institutional Training Program (T32)

Mentored Career Development Program (K01, K08, K23, K25)

Individual Pre-doctoral and Post-doctoral Fellowships (F30, F31, F32)

Mental Health Education Program (R25)

Dissertation Research Grants to Increase Diversity (R36)

### **Areas of Emphasis**

See individual Branch and program descriptions below.

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## Traumatic Stress Research Program (AD-TS)

The Traumatic Stress Research Program is the DATR/NIMH point of contact for disaster/terrorism/biodefense-related research. The program supports research on biopsychosocial risk/protective factors for psychopathology after traumatic events and the development of interventions for PTSD in adults; and research spanning and integrating basic science, clinical practice, and health care system factors regarding mass trauma and violence (e.g. war, terrorism, natural and technological disaster), including interventions and service delivery targeting an array of relevant mental health concerns (distress, disorder, functional sequelae) in children, adolescents, and adults.

### Areas of Emphasis

- Studying genetic and environmental interactions that cause posttraumatic disorders.
- Developing highly predictive early diagnostics for PTSD.
- Developing effective and feasible psychosocial and pharmacological interventions for fear extinction to prevent chronic PTSD.
- Mapping neurohormonal, physiological, and behavioral parameters in PTSD development that predict treatment seeking, adherence, and outcome.
- Developing cost-effective identification and treatment approaches for posttraumatic distress and psychopathology in non-mental health settings.

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## **Adult Psychopathology and Psychosocial Intervention Research Branch (A2-AI)**

This Branch supports research on the foundations of psychopathology and its associated disability. The Branch promotes translational research that is directed toward an understanding of how the development, onset, and course of adult psychopathology may be studied in terms of dysfunction in fundamental biobehavioral mechanisms such as emotion, cognition, motivational processes, and interpersonal relationships. The program includes research on modifiable risk and protective factors for disorder and on the use of modern psychometric techniques to guide refinements in the conceptualization and assessment of disorder. Emphasis is placed on studies that combine approaches from neuroscience and behavioral science to elucidate the role of psychosocial factors in the alterations of brain functioning associated with mental disorders and to produce integrative models of risk, disorder, and recovery. An important feature of the Branch is the support of interdisciplinary basic research on emotion, mood, temperament, and motivational systems that is explicitly conceived and designed with respect to its potential for direct translation to the psychopathology of disorders, and to the development of new preventive and treatment interventions. The overarching goal is to foster new science-based behavioral strategies for assessment, prevention, treatment, and recovery.

### **Branch Programs**

Mood, Sleep, and Eating Disorders Research Program (A2-AID)

Psychopathology Risk and Protective Factors Research Program (A2-AIE)

Psychopathology, Behavioral Dysregulation, and Measurement Development Research Program (A2-AII)

Schizophrenia Spectrum Disorders Research Program (A2-AISZ)

Affective Processes and Anxiety Disorders Research Program (A2-AIA)

Psychosocial Intervention Efficacy Research Program (A2-AIR)

### **Areas of Emphasis**

- Identifying phenotypes and endophenotypes as new targets for assessment and therapeutics, that are emerging from integrative genetics, pathophysiology, and psychopathology research.
- Conducting translational research on emotion and affect dysregulation to find new strategies for treating disorders of anxiety and mood.
- Identifying ways in which genetic and environmental factors interact to raise or lower risk for mental disorders.
- Developing new preventive and treatment interventions targeted to specific cognitive, emotional, or interpersonal components of the psychopathology of disorder.
- Using modern psychometric and statistical theories to advance fundamental conceptualizations of nosology and consequent approaches toward more focused assessment and treatment of the many dimensions and subtypes that constitute complex psychiatric disorders.

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### **Mood, Sleep, and Eating Disorders Research Program (A2-AID)**

This program supports research on the etiology, core features, longitudinal course, and assessment of mood, sleep, and eating disorders. It also supports studies focusing on the elucidation of risk factors for the onset or recurrence of psychopathology. Intervention development studies grounded in findings from psychopathology are supported as the next step in the translation of basic research to effective treatments.

#### **Areas of Emphasis**

See the Branch description above.

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### **Psychopathology Risk and Protective Factors Research Program (A2-AIE)**

This program supports research on the determinants and distributions of mental disorders in the population. To that end it supports research on the etiology of psychiatric disorders and the identification of risk and protective factors that precede the onset of mental illness; on the development of empirically based prevention and intervention strategies based on risk factor research; on the development of standardized assessments of psychiatric disorders, endophenotypes, and environmental factors; and on estimations of the prevalence and impact of psychiatric disorders in the general population.

#### **Areas of Emphasis**

See the Branch description above.

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### **Psychopathology, Behavioral Dysregulation, and Measurement Development Research Program (A2-AII)**

This program supports research on phenotypic structures that underlie psychopathology and contribute directly to mental disorders and impaired functioning, and on the development of interventions to change or moderate these structures; on the dysregulated behavioral and emotional processes that comprise the psychopathology of personality disorders, and related intervention development studies grounded in findings from psychopathology research; and on the development of statistical methodologies and state-of-the-art measures (using modern psychometrics) for psychopathology constructs, disorders, symptoms, and moderators and mediators of intervention.

#### **Areas of Emphasis**

See the Branch description above.

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### **Schizophrenia Spectrum Disorders Research Program (A2-AISZ)**

This program supports research into the origins, onset, course, and outcome of schizophrenia, schizoaffective disorder, and such related conditions as schizotypal and schizoid personality disorders. The goals of the program are to discover mechanisms that transform vulnerability characteristics into active illness; to identify valid markers of illness onset; to develop psychometrically sound methods for assessing the cognitive, affective, and behavioral response systems believed to underpin clinical symptoms and functional impairments; and ultimately to channel scientific findings from each of these areas into the development of effective methods of mental illness prevention, treatment, and rehabilitation.

#### **Areas of Emphasis**

See the Branch description above.

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### **Affective Processes and Anxiety Disorders Research Program (A2-AIA)**

This program supports translational research on the etiology and course of anxiety disorders, including research aimed at an improved understanding of the similarities and differences in psychopathology among different anxiety disorders. It also encourages research on emergent preventive and treatment interventions. Research on affective processes may be basic or translational and may be conducted from a behavioral or integrative perspective. Topic areas of basic research include emotion, motivation, temperament/personality, and social affective processes that contribute to an enhanced understanding of risks for disorders and to new approaches for preventive or treatment interventions.

#### **Areas of Emphasis**

See the Branch description above.

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### **Psychosocial Intervention Efficacy Research Program (A2-AIR)**

This program supports trials to evaluate the efficacy of psychosocial preventive and treatment interventions across all areas of adult mental disorders, including studies of established psychosocial interventions that are being applied to a different disorder for which efficacy has not yet been demonstrated. Studies which incorporate measures to study mechanisms of therapeutic change (psychosocial or biological), predictors of outcome, and multi-modal assessment of treatment outcome are particularly encouraged.

## Areas of Emphasis

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## Clinical Neuroscience Research Branch (A3-NS)

The Clinical Neuroscience Research Branch supports programs of research, research training, and resource development aimed at understanding the neural basis of mental disorders. Specifically supported are human and animal studies on the molecular, cellular, and systems level of brain function designed to elucidate the pathophysiology of mental disease and to translate these findings to clinical diagnosis, treatment, and prevention strategies. These approaches are applied to a spectrum of mental disorders including schizophrenia, depression, bipolar disorder, anxiety disorder, and other brain disorders. The Branch incorporates the Clinical Neuroscience Centers Program, which is focused on translational research. The Silvio O. Conte Centers for the Neuroscience of Mental Disorders support hypothesis-driven, interdisciplinary research centers, each of which brings the best scientific talent and resources from multiple disciplines and perspectives to address specific questions directly relevant to complex mental disorders.

## Branch Programs

Molecular and Cellular Psychopathology Program (NS-M)

Neural Systems Psychopathology Program (NS-S)

Clinical Neuroscience Centers Program (NS-C)

## Areas of Emphasis

- Identification of valid and unique neurophysiological markers or complex(es) of markers for the major mental and personality disorders.
- Development of animal and/or computational models that accurately mimic complex neurophysiology or behaviors characteristic of mental illness.
- Comparisons between CNS characteristics of mental disorders and “other” brain disorders sharing specific abnormal behaviors or symptoms.
- Examination of how complex interactions between neural signaling systems may readjust behavior from functional to dysfunctional.
- Promotion of the application of exploratory but potentially relevant neuroscience areas to the study of mental disorders.

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## Molecular and Cellular Psychopathology Program (A3-NSM)

This program supports research seeking to understand the neuroscience of psychopathology at a molecular and/or cellular level; its goal is to reveal how direct and/or indirect alterations of

molecular pathways (resulting in abnormal signal transduction, neural/synaptic plasticity, development, hormonal and homeostatic regulation, etc.) lead to symptoms or symptom complexes that are characteristic of mental disorders. Appropriate applications may employ tissue culture, animal models, electrophysiology, neurochemistry, neuroendocrinology, genetic approaches, studies of human postmortem tissue, and/or neuroimaging to elucidate the neural systems involved in major mental illnesses, personality disorders, or abnormal behaviors.

#### Areas of Emphasis

See the Branch description above.

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### **Neural Systems Psychopathology Program (A3-NSS)**

This program supports research that seeks to understand the neuroscience of psychopathology at a systems level; it focuses on how the integration of multiple neural signals, circuits and/or structures lead to symptoms or symptom complexes that are characteristic of mental disorders. Appropriate applications may employ animal models, neuroimaging, electrophysiology, neurochemistry, neuroendocrinology, and/or genetic approaches to elucidate the neural systems involved in major mental illnesses, personality disorders, or abnormal behaviors.

#### Areas of Emphasis

See the Branch description above.

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### **Clinical Neuroscience Centers Program (A3-NSC)**

This program supports translational research centers that seek to promote bi-directional scientific translation from the bench to bedside and back; it aims to promote novel scientific discovery and cross-pollination of ideas and disciplines through a program of centers, each of which has a narrow, mechanistic, hypothesis-driven focus and consists of a series of multidisciplinary, interdependent projects seeking to elucidate the etiology, pathophysiology, and pathogenesis of a major mental disorder(s). The feasibility of establishing a network of these centers—to accelerate the pace of discovery—is currently being evaluated.

#### Areas of Emphasis

See the Branch description above.

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## **Geriatrics Research Branch (A4-GP)**

The Geriatrics Research Branch supports programs of research, research training, and resource development in the etiology and pathophysiology of mental disorders of late life, the treatment and recovery of persons with these disorders, and the prevention of these disorders and their consequences. The program encourages collaborative multidisciplinary research programs using the tools of molecular neuroscience, cognitive sciences, and social and behavioral sciences to facilitate the translation of basic science and preclinical research to clinical research. Studies may involve use of brain imaging, pharmacogenetics and genomics, and molecular biology related to neurodegenerative and neuropsychiatric disorders of aging. Disorders include: Alzheimer's disease and related dementias; psychotic disorders and schizophrenia; mood, anxiety, and personality disorders; suicide; neuroregulatory disorders and homeostatic disorders including sleep disorders, eating disorders, and disorders associated with the menstrual cycle.

### **Branch Programs**

Geriatric Translational Behavioral Science Program (A4-GPB)

Geriatric Psychosocial Treatment Intervention Program (A4-GPS)

Geriatric Multi-modality Intervention Program (A4-GPM)

Geriatric Translational Neuroscience Program (A4-GPT)

Geriatric Pharmacologic Intervention Program (A4-GPX)

Geriatric Research Resources Office (A4-GPC)

### **Areas of Emphasis**

See specific program descriptions below.

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## **Geriatric Translational Behavioral Science Program (A4-GPB)**

This program supports studies of risk factors, presentation, course, and outcome of late-life mental disorders using tools of the basic and translational social and behavioral sciences and clinical geropsychology; it supports use of these tools as correlates, modifiers, mediators, and predictors of treatment response variability.

### **Areas of Emphasis**

- Studies of behavioral, cognitive and social factors contributing to older adults' vulnerability/resilience to mental disorders and associated disability.
- Studies that identify behavioral, cognitive and social correlates, predictors, and mechanisms of treatment response variation in late-life mental disorders.
- Studies developing and testing more reliable and valid phenotypes, assessments, and behavioral markers for late-life mental disorders.

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#### **Geriatric Psychosocial Treatment Intervention Program (A4-GPS)**

This program supports experimental and observational studies of the development and testing of behavioral and psychosocial interventions for the treatment, prevention, or rehabilitation of the mental disorders of late life. Acute, continuation, and maintenance approaches are evaluated. Program includes studies of relapse prevention and enhancement of function/reduction of disability.

#### Areas of Emphasis

- Research to develop and pilot-test new or adapted psychosocial treatment approaches, including those to enhance older adults' access to, acceptance of, and adherence to empirically supported treatment approaches.
- Studies testing the efficacy and effectiveness of psychosocial interventions for producing specific clinical outcomes.
- Research clarifying the key treatment conditions and change mechanisms involved in efficacious psychosocial interventions for late-life mental disorders.

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#### **Geriatric Multi-Modality Intervention Program (A4-GPM)**

This program supports experimental and observational studies of the development and testing of strategies combining pharmacologic or somatic interventions with behavioral or psychosocial interventions for the treatment, prevention, or rehabilitation of the mental disorders of late life. Protocols include combination, augmentation, sequential, and switching strategies. Acute, continuation, and maintenance approaches are evaluated. Program includes studies of relapse prevention and enhancement of function/reduction of disability.

#### Areas of Emphasis

- Studies comparing the time-course and benefits of treatment modalities, stressing completeness and durability of clinical and functional improvements.
- Studies testing sequential algorithms for combining or changing interventions to address inadequate treatment response and/or residual symptoms.
- Studies of optimal ways to combine or sequence interventions to address the multiple treatment needs of patients with comorbid conditions.

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### **Geriatric Translational Neuroscience Program (A4-GPT)**

This program supports studies of risk factors, presentation, course, and outcome of late-life mental disorders using tools of the basic and translational neurosciences and cognitive sciences. It supports use of these tools as correlates, modifiers, mediators, and predictors of treatment response variability.

#### **Areas of Emphasis**

- Studies to understand the aging-related processes damaging or protecting brain structures that predispose to psychiatric disorders.
- Studies to understand the mechanisms mediating psychiatric symptom expression in elderly patients.
- Research examining the interaction of genetic and environmental factors that may be protective for the development of late-life mental disorders.

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### **Geriatric Pharmacologic Intervention Program (A4-GPX)**

This program supports experimental and observational studies of the development and testing of pharmacologic and somatic interventions for the treatment, prevention, or recovery from the mental disorders of late life. Acute, continuation, and maintenance approaches are evaluated. The program includes studies of relapse prevention and enhancement of function/reduction of disability.

#### **Areas of Emphasis**

- Mechanisms of action, tolerability, and safety of psychiatric medications in late-life mental illness and any age-related changes in mechanisms.
- Effectiveness studies of the use of pharmacologic and behavioral treatments in treating late-life disorders in at-risk populations.
- Treatment/prevention studies targeting the major neurotransmitter system abnormalities of vulnerability pathways for psychiatric disorders.

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### **Geriatric Research Resources Office (A4-GPC)**

This Office supports special projects and mechanisms to enhance research on late-life mental disorders, including research centers, research workshops and conferences, and coordinating centers for multi-site studies.

#### **Areas of Emphasis**

See specific program descriptions above.

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## **Experimental Therapeutics Branch (A5-ET)**

The Experimental Therapeutics Branch supports multidisciplinary programs of research, research training, and resource development on: novel pharmacological approaches to the treatment of mental disorders; the evaluation of existing treatments for new clinical indications; the validation and assessment of the clinical utility of putative biomarkers of disease presence or extent in the context of treatment trials; studies designed to clarify the mechanisms and define predictors of both therapeutic treatment response and side effects of psychotropic medications; and the development and testing of novel somatic treatments. The Branch supports cross-institute activities to identify specific bottlenecks in the development of novel treatments for mental disorders and collaborates with academic, industry, and regulatory agencies to develop programmatic approaches to hasten the availability of better treatments to reduce the burden of mental illness.

### **Branch Programs**

Psychotic Disorders Treatment Development Program (ET-PD)

Mood and Anxiety Disorders Treatment Development Program (ET-MA)

Side Effects of Psychiatric Therapeutics Program (ET-SE)

### **Areas of Emphasis**

- Early-phase clinical studies of new medications targeting major mental illnesses or symptom domains now lacking adequate treatments.
- Studies integrating evaluation of mechanisms of therapeutic response to pharmacological agents with assessment of efficacy.
- Studies to predict treatment response and facilitate individualized pharmacological therapeutics.
- Clinical treatment studies integrating biomarkers with traditional clinical endpoints to validate the clinical utility of putative surrogate markers of treatment response.
- Studies to identify predictors of adverse effects of psychopharmacological agents and intervention development to mitigate these adverse effects.
- Studies of efficacy of novel somatic treatments or medical devices for the treatment of mental illness.

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## **Psychotic Disorders Treatment Development Program (A5-ETPD)**

This program supports studies of novel psychopharmacological and somatic approaches to alleviating the full spectrum of symptom domains found in patients with schizophrenia and schizophrenia spectrum disorders, including positive symptoms, deficit symptoms, disorganization, and cognitive deficits associated with these conditions. The program also supports studies that integrate investigations of the mechanisms of treatment response with efficacy of treatments, and studies designed to develop biomarkers and other predictors of treatment response for these conditions.

### **Areas of Emphasis**

See the Branch description above.

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#### **Mood and Anxiety Disorders Treatment Development Program (A5-ETMA)**

This program supports studies of novel psychopharmacological and somatic approaches to alleviating the full range of symptoms associated with mood and anxiety disorders, including affective spectrum conditions, bipolar disorder, obsessive-compulsive disorder, post-traumatic stress disorders, and other psychiatric conditions. The program also supports studies that integrate investigations of the mechanism of treatment response with efficacy of treatments, and studies designed to develop biomarkers and other predictors of treatment response for these conditions.

#### Areas of Emphasis

See the Branch description above.

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#### **Side Effects of Psychiatric Therapeutics Program (A5-ETSE)**

This program supports research to elucidate the biomedical and psychosocial risk factors for the development of treatment-emergent side effects of psychiatric therapeutics, and to develop interventions to predict, prevent and/or mitigate these side effects.

#### Areas of Emphasis

See the Branch description above.

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